PATENT SPECIFICATION

NO DRAWINGS

1,128,382

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Date of Application and filing Complete Specification: 6 May, 1966.
No. 20090/66.
Application made in Germany (No. F45971 IVd/12p) on 6 May, 1965.
Complete Specification Published: 25 Sept., 1968.

Index at acceptance:—C2 C(1J1A1, 1J1A3, 1J1A6, 1J1B, 1J1C2, 1J1C3, 1J12, 1Q5, 1Q6C, 1Q7A, 1Q8A, 1Q9A, 1Q9H, 1Q11G, 1Q11J, 2D43B, 2D43D, 2D43F, 2D43S2, 2D43S4, 2D43Z1, 2D48)

Int. Cl.:—C 07 c 143/78, C 07 d 25/00, C 07 d 27/04, C 07 d 29/34, C 07 d 31/24, C 07 d 41/04, C 07 d 43/18, C 07 d 99/06

COMPLETE SPECIFICATION

New Benzene-Sulphonyl Semicarbazides and preparations containing them

[redacted] Vormals Meister Lucius &

ERRATA

SPECIFICATION No. 1,128,382

Page 1, line 4, *for* "peerformed" *read* "performed"
Page 3, line 23, centre Formula, *for* indistinct letters *read* "Br"
Page 4, line 5, centre Formula, *for* indistinct letters *read* "CH=CH—"
Page 7, line 13, *for* "diabetis" *read* "diabetes"
Page 8, lines 38 and 39, *after* "benzene-sulphonyl]" *delete* hyphen (second occurrence)
Page 9, line 12, *for* indistinct word *read* "ethyl)"
Page 12, line 3, *for* "γ-(ethyl-" *read* "(γ-ethyl-"
Page 15, line 14, *for* "R_1" *read* "R^1"

THE PATENT OFFICE
4th November 1968

[redacted]

Y represents a $-CH_2-CH_2-$ or $-CH_2-CH(CH_3)-$ group

R^1 represents

(a) an alkylene - imino radical containing from 3 to 7 carbon atoms wherein the alkylene chain may be substituted by 2 to 4 methyl groups or by an alkyl or alkoxy radical containing up to 3 carbon atoms, or,

(b) an aliphatic hydrocarbon imino radical containing 5 carbon atoms which is unsaturated or contains an endoalkylene group having from 1 to 3 carbon atoms which may be substituted by lower alkyl or lower alkoxy, or

[*Price 4s. 6d.*]

SEE ERRATA SLIP ATTACHED

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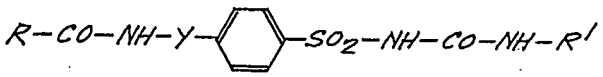
COMPLETE SPECIFICATION

New Benzene-Sulphonyl Semicarbazides and preparations containing them

We, FARBWERKE HOECHST AKTIENGESELLSCHAFT, Vormals Meister Lucius & Brüning, a Company recognised by German law, of 6230 Frankfurt (M)-Hoechst, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be peerformed, to be particularly described in and by the following statement: —

The present invention provides compounds of the formula



wherein R represents

(a) a phenyl radical which may be unsubstituted or contain up to 3 substituents selected from lower alkyl, lower alkenyl, lower alkoxy, lower alkenoxy and lower alkoxyalkoxy radicals, halogen atoms and methylenedioxy and trifluoromethyl,

(b) a thienyl radical which may be unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and lower alkyl, lower alkoxy, lower alkenyloxy, lower alkoxyalkoxy, phenyl - lower alkoxy and aryl radicals or by a polymethylene chain linked at its two ends to the thienyl radical, which chain contains 3 or 4 carbon atoms,

(c) a furyl radical which may be unsubstituted or substituted by one or more substituents selected from halogen atoms and methyl groups,

(d) a phenyl radical bound via a saturated or unsaturated branched or unbranched aliphatic hydrocarbon chain containing from 1 to 4 carbon atoms which may contain an oxygen atom instead of one CH_2-group, the phenyl radical containing, if desired, one or more substituents selected from halogen atoms and lower alkyl or lower alkoxy radicals,

(e) a cyclohexyl or cyclohexenyl radical, or

(f) an alkyl radical containing from 1 to 11 carbon atoms, or an unsaturated aliphatic hydrocarbon radical containing from 2 to 11 carbon atoms,

Y represents a $-CH_2-CH_2-$ or $-CH_2-\underset{\displaystyle CH_3}{\underset{|}{CH}}-$ group

R^1 represents

(a) an alkylene - imino radical containing from 3 to 7 carbon atoms wherein the alkylene chain may be substituted by 2 to 4 methyl groups or by an alkyl or alkoxy radical containing up to 3 carbon atoms, or,

(b) an aliphatic hydrocarbon imino radical containing 5 carbon atoms which is unsaturated or contains an endoalkylene group having from 1 to 3 carbon atoms which may be substituted by lower alkyl or lower alkoxy, or

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(c) the radical $-N<^{R_1}_{R_2}$, wherein R_1 represents a lower alkyl radical, and R_2 represents a lower alkyl or benzyl radical.

The term "lower" in qualifying groups or radicals is used herein to mean those groups and radicals having up to 4 carbon atoms.

The invention also provides physiologically tolerable salts of such compounds. The compounds of the above formula and their physiologically tolerable salts are new compounds.

The present invention also provides a process for preparing the benzenesulphonyl semicarbazides of the above formula. As methods of preparation there may be mentioned the following:

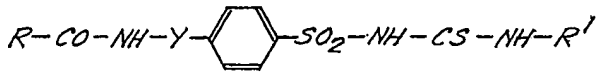
(a) Reaction of an R—CO—NH—Y substituted benzenesulphonamide, preferably in the form of a salt, with an R^1-substituted carbamic acid ester, thiocarbamic acid ester or urea,

(b) reaction of a hydrazine of the formula $R^1—NH_2$ or a salt thereof with an R—CO—NH—Y - substituted benzenesulphonyl isocyanate, benzenesulphonyl carbamic acid ester or benzenesulphonyl thiocarbamic acid ester, carbamic acid halide or urea,

(c) reaction of an R—CO—NH—Y-substituted benzenesulphochloride with an R^1-substituted urea,

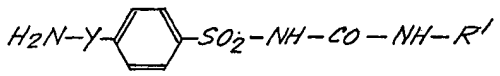
(d) hydrolysis of a benzenesulphonyl - isosemicarbazide ether or -isothiosemicarbazide ether or 1 - benzenesulphonyl - 3 - R^1 - parabanic acid,

(e) exchange of the sulphur atom for an oxygen atom in a known manner in a benzenesulphonyl thiosemicarbazide of the formula



and

(f) introduction of the radical R—CO— in one or several steps, into benzenesulphonyl semicarbazide of the formula



by acylation.

The benzenesulphonyl semicarbazides obtained may then be converted, if desired, into their physiologically tolerable salts by treatment with suitable alkaline agents or with suitable inorganic or organic acids.

As R^1-substituted-ureas for the syntheses mentioned under (a), there are suitable compounds of the formula $R^1—NH—CO—NH_2$ or acylated compounds of the formula $R^1—NH—CO—NH$-acyl wherein acyl represents an aliphatic or aromatic acid radical, preferably of lower molecular weight, or diphenyl semicarbazides of the formula $R^1—NH—CO—N(C_6H_5)_2$, wherein the phenyl radicals may be substituted or may be linked to each other directly or by means of a bridge member, or N,N′ - disubstituted carbohydrazides of the formula $R^1—NH—CO—NH—R^1$.

Especially suitable as benzenesulphonyl carbamic acid halides are the chlorides.

Furthermore, corresponding benzenesulphonyl ureas which may be unsubstituted at the terminal nitrogen atom, or substituted by one or two substituents selected from alkyl and aryl groups, may be converted into the final products by reacting them with hydrazines of the formula $R^1—NH_2$, if desired in the form of their salts. Instead of these benzenesulphonyl ureas there may be used the corresponding N - benzenesulphonyl - N′ - acyl ureas or bis - (benzenesulphonyl) - ureas. These compounds may be treated with hydrazines of the formula $R^1—NH_2$ and the salts obtained may be heated to elevated temperatures, preferably to at least 80°C.

The R^1-substituted carbamic acid esters or bezenesulphonyl carbamic acid esters mentioned, as well as the corresponding thioesters, preferably contain an alkyl radical of low molecular weight or a phenyl radical in the ester component.

The benzenesulphonyl isosemicarbazide ethers, -isothiosemicarbazide ethers or -parabanic acids used as starting materials, may be obtained by reacting a corresponding isosemicarbazide ether, isothiosemicarbazide ether or parabanic acid with a corres-

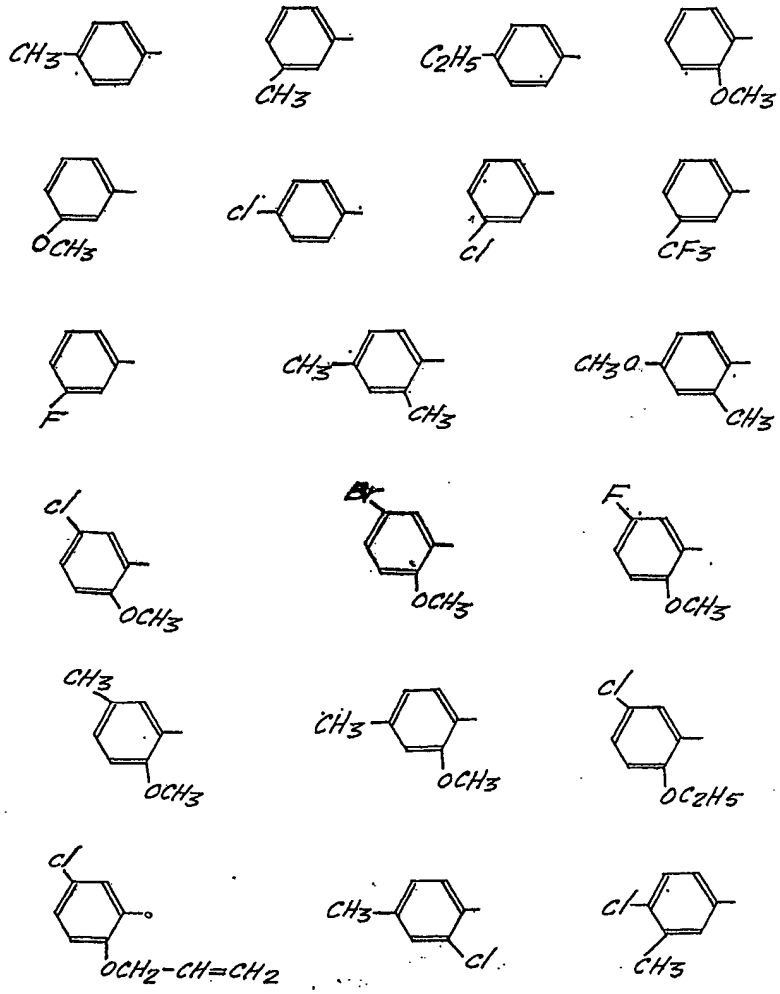
ponding benzenesulphochloride. Benzenesulphonyl isosemicarbazide ethers are also obtained, in the first place, by desulphurizing benzenesulphonyl thiosemicarbazides in a known manner in methanolic solution. They are subsequently converted into benzenesulphonyl semicarbazides by hydrolysis.

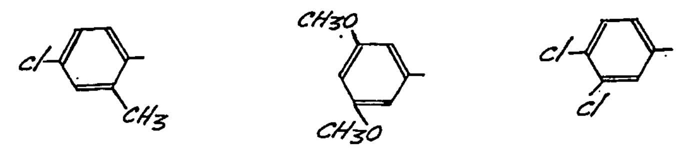
Depending on the nature of the member R—CO—, in some cases, the one or the other of the previously described methods may prove unsuitable for preparing the individual compounds falling under the general formula, or at least will make it necessary for active groups to be protected. Such rare cases can easily be recognized by the expert, and there is no difficulty in successfully applying another one of the syntheses described.

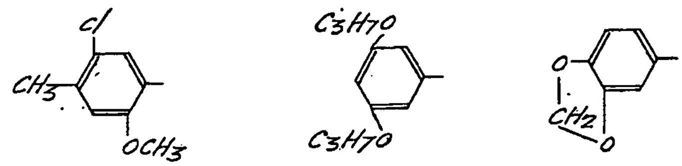
As regards the reaction conditions, the forms of the process of the present invention may, in general, vary within wide limits and may be adapted to each individual case. For example, the reactions can be effected with the use of solvents, at room temperature or at an elevated temperature. As starting substances there are used, as one reactant, compounds containing a benzene radical substituted by the group

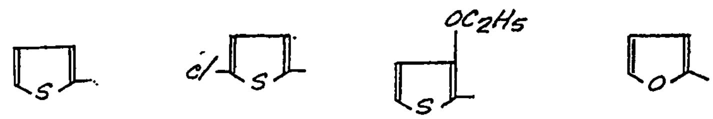
R—CO—NH—Y—.

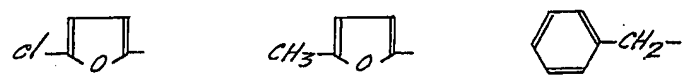
As radical R may be mentioned, for example, the following groups:

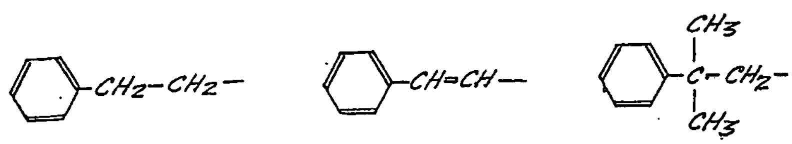


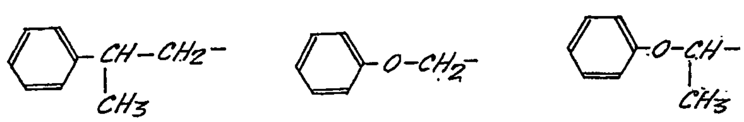


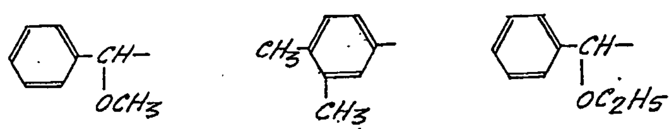


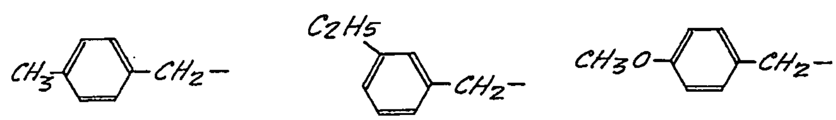






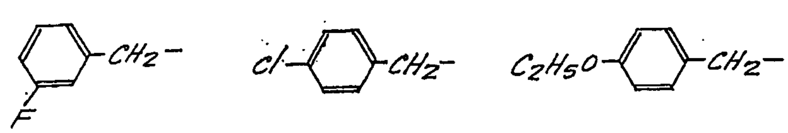




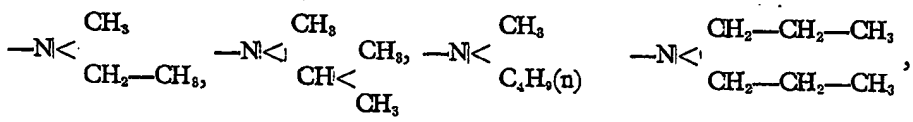


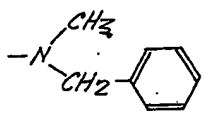
$CH_3—$, $C_2H_5—$, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH—$, $CH_3—CH_2—CH_2—$, $CH_3—(CH_2)_8—CH_2—$,

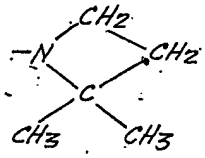
$CH_3—(CH_2)_5—CH_2—$, $CH_3—(CH_2)_7—CH_2—$, $CH_2{=}CH—$, $CH_3—CH{=}CH—$,

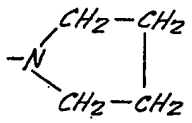


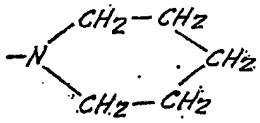
R^1 may represent, for example:

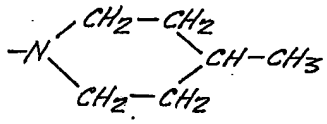


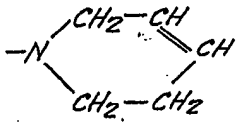


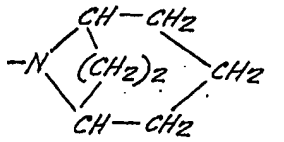


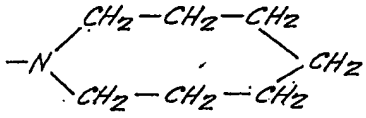


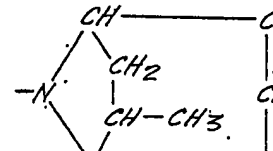


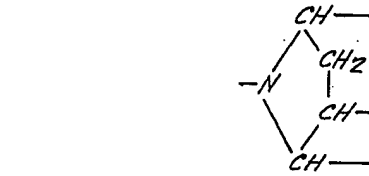


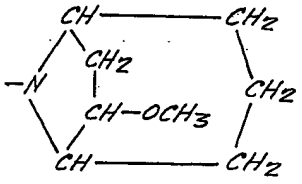












The sulphonyl - semicarbazide derivatives of the present invention and their physiologically tolerable salts are valuable medicaments which are distinguished by a strong and particularly long lasting action of lowering the blood sugar level. This applies, more especially, to such compounds in which R represents a phenyl radical carrying an alkoxy group in 2-position. The blood sugar lowering action of the products of the invention can be ascertained, for example, in rabbits, by administering the compounds in a dose of 10 mg/kg and by determining the blood sugar value, over a prolonged period of time, according to the known method of Hagedorn-Jensen. The following table comprises the blood sugar lowering activities of some of the compounds obtained according to the process of the present invention:

Compound	Lowering of the blood sugar in rabbits after administering 10 mg/kg per os after		Limit amount causing lowering of the blood sugar level in rabbits	
	3 hours	24	48	mg/kg
4-[4-(β-<β-phenyl-propionamido>-ethyl)-benzenesulphonyl]-1,1-pentamethylene-semi-carbazide	26%	22%	—	0.15
4-[4-(β-<2-Propoxy-benzamido>-ethyl-benzenesulphonyl]-1,1-(γ-methyl-pentamethylene)-semicarbazide	17%	42%	—	0.07
4-[4-(β-<2-Methoxy-5-chlorobenzamido>-ethyl)-benzenesulphonyl]-1,1-pentamethylene-semicarbazide	32%	20%	—	0.2
4-[4-(β-<2-Methoxy-5->chlorobenzamido-ethyl)-benzenesulphonyl]-1,1-hexamethylene-semicarbazide	28%	22%	31%	0.06
4-[4-(β-<2-Methoxy-4-chlorobenzamido>-ethyl)-benzenesulphonyl]-1,1-(γ-methyl-pentamethylene)-semicarbazide	26%	29%	7%	0.15
4-[4-(β-<2-Methoxy-5-methyl-benzamido>-ethyl)-benzenesulphonyl]-1,1-(γ-methyl-pentamethylene)-semicarbazide	30%	35%	—	0.05
4-[4-(β-<2-Methoxy-ethoxy-5-methyl-benzamido>-ethyl)-benzenesulphonyl]-1,1-(γ-methyl-pentamethylene-) semicarbazide	25%	31%	—	0.2
4-[4-(β-<2-Methoxy-benzamido>-ethyl)-benzenesulphonyl]-1,1-pentamethylene-semicarbazide	20%	7%	—	0.03

In contradistinction thereto, N - (4 - methyl - benzenesulphonyl) - N′ - n - butyl-urea which is known as an antidiabetic compound and is used as medicament shows no lowering of the blood sugar level when administered in a dose of 25 Mg/kg in a comparative test.

The products of the present invention are preferably made up into orally administerable preparations which have blood sugar lowering action and which can accordingly be used in the treatment of diabetes mellitus; they can be employed as such or in the form of their physiologically tolerable salts or in the presence of substances causing salt formation. For such salt formation there can be used, for example, alkaline agents such, for example, as alkali metal hydroxides, alkaline earth metal hydroxides, alkali metal carbonates, alkaline earth metal carbonates, alkali metal bicarbonates and alkaline earth metal bicarbonates and physiologically tolerated acids. The pharmaceutical preparations are preferably in the form of tablets which contain, in addition to the compounds of the present invention, the usual adjuvants and carriers such, for example, as talc, starch, lactose, tragacanth and magnesium stearate.

Accordingly, the present invention also provides a pharmaceutical preparation for oral administration and lowering the blood sugar level in the treatment of diabetis mellitus, which comprises a compound of the invention or physiologically tolerable salt thereof, in admixture or conjunction with a pharmaceutically suitable carrier.

The following Examples illustrate the present invention:

EXAMPLE 1

(a) 4 - [4 - (β - ⟨3 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide

10 Grams of N - [4 - (β - ⟨3 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane (m.p. 173—175°C) were suspended in 100 ml of dioxane and 2.8 grams of 1,1 - pentamethylene - hydrazine were added while stirring. The mixture was heated to 120—130°C for an hour while the methanol, formed during the reaction process, was distilling off together with a little amount of dioxane. Upon being cooled, the 4 - [4 - (β - ⟨3 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide formed precipitated in crystalline form and was purified by dissolving it in dilute ammonia and by subsequently precipitating it with dilute acetic acid. After recrystallization from methanol and dimethyl formamide, the semicarbazide melted at 229—231°C (decomposition).

In analogous manner there were obtained:

b) 4 - [4 - (β - ⟨3 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 207—209°C (decomposition) (from methanol/dimethyl formamide) and

(c) 4 - [4 - (β - ⟨3 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1 - methyl-1 - benzyl - semicarbazide, m.p. 112—114°C (decomposition) (from methanol/water);

from N - [4 - (β - ⟨4 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl-urethane, m.p. 213—215°C,

d) 4 - [4 - (β - ⟨4 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 220—223°C (decomposition) from dimethyl formamide/water and

e) 4 - [4 - (β - ⟨4 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 195—198°C (decomposition) (from dimethyl formamide/methanol);

from N - [4 - (β - ⟨4 - fluoro - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl urethane, m.p. 194—196°C

f) 4 - [4 - (β - ⟨4 - fluoro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 238—240°C (decomposition) (from methanol/dimethyl formamide) and

g) 4 - [4 - (β - ⟨4 - fluoro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 208—210°C (decomposition) (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨3 - methyl - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 200—202°C

h) 4 - [4 - (β - ⟨3 - methyl - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 241—243°C (decomposition (from methanol/di - methyl formamide) and

i) 4 - [β - ⟨3 - methyl - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 209—211°C (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 174—176°C

k) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 157—159°C (from methanol),

l) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexa-

methylene - semicarbazide, m.p. 155—157°C (from methanol) and
m) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1-tetramethylene - semicarbazide, m.p. 172—174°C (from methanol/dimethyl formamide);
from N - [4 - (β - ⟨3 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 173—175°C
n) 4 - [4 - (β - ⟨3 - methoxy - benzamido⟩ - ethyl) - benezenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 230—232°C (decomposition) (from methanol/dimethyl formamide); and
o) 4 - [4 - (β - ⟨3 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 207—209°C (decomposition) (from methanol/dimethyl formamide);
from N - [4 - (β - ⟨2 - allyloxy - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 145—148°C
p) 4 - [4 - (β - ⟨2 - allyloxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 157—159°C (from methanol);
from N - [4 - (β - ⟨2 - methoxy - 5 - methyl - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 175—177°C
q) 4 - [4 - (β - ⟨2 - methoxy - 5 - methyl - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 176—178°C (decomposition) from methanol);
from N - [4 - (β - ⟨β - phenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 137—139°C
r) 4 - [4 - (β - ⟨β - phenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 173—175°C (decomposition) (from methanol);
from N - [4 - (β - ⟨3 - trifluoromethyl - benzamido⟩ - ethyl) - benzenesulphonyl] - methylurethane, m.p. 178—180°C
s) 4 - [4 - (β - ⟨3 - trifluoromethyl - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1-pentamethylene - semicarbazide, m.p. 209—211°C (decomposition) from methanol/dimethyl formamide) and
t) 4 - [4 - (β - ⟨3 - trifluoromethyl - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1-hexamethylene - semicarbazide, m.p. 201—202°C (from methanol/dimethyl form - amide);
from N - [4 - (β - ⟨3 - methoxy - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 226—228°C (decomposition)
u) 4 - [4 - (β - ⟨3 - methoxy - thiophene - 2 - carbamido⟩ - ethyl) - benzene - sulponyl] - 1,1 - pentamethylene semicarbazide, m.p. 202—204°C (from methanol/dimethyl formamide) and
v) 4 - [4 - (β - ⟨3 - methoxy - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 181—182°C (from methanol/dimethyl formamide);
from N - [4 - (β - ⟨phenoxy - acetamido⟩ - ethyl) - benzenesulphonyl] - methyl-urethane, m.p. 136—138°C
w) 4 - [4 - (β - ⟨phenoxy - acetamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 150—151°C (from methanol),
x) 4 - [4 - (β - ⟨phenoxy - acetamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 111—113°C (from methanol) and
y) 4 - [4 - (β - ⟨phenoxy - acetamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3-methylpentamethylene) - semicarbazide, m.p. 153—155°C (from methanol);
from N - [4 - (β - ⟨β - phenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 142—144°C
z) 4 - [4 - (β - ⟨β - phenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 148—150°C (from methanol),
aa) 4 - [4 - (β - ⟨β - phenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - tetramethylene - semicarbazide, m.p. 167—168°C (from methanol),
ab) 4 - [4 - (β - ⟨β - phenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1 - methyl - 1 - benzyl - semicarbazide, m.p. 158—160°C (from methanol) and
ac) 4 - [4 - (β - ⟨β - phenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3-methyl - pentamethylene) - semicarbazide, m.p. 180—182°C (from methanol);
from N - [4 - (β - ⟨cinnamoylamino⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 198—200°C
ad) 4 - [4 - (β - ⟨cinnamoylamino⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methylpentamethylene) - semicarbazide, m.p. 198—200°C (from methanol/dimethyl formamide);
from N - [4 - (β - ⟨Δ^3 - tetrahydro - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 151—153°C

ae) 4 - [4 - (β - ⟨Δ³ - tetrahydro - benzamido⟩ - ethyl) - benzenesulphonyl - 1,1 - hexamethylene - semicarbazide, m.p. 170—171°C (decomposition) (from methanol) and

af) 4 - [4 - (β - ⟨Δ³ - tetrahydro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3-methyl - pentamethylene) - semicarbazide, m.p. 184—186°C (decomposition) (from methanol)

from N - [4 - (β - ⟨3 - trifluoromethyl - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 178—180°C

ag) 4 - [4 - (β - ⟨3 - trifluoromethyl - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1-(3 - methyl - pentamethylene) - semicarbazide, m.p. 222—224° (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨3 - fluorobenzamido - ethyl) - benzenesulphonyl] - methyl-urethane, m.p. 184—186°C

ah) 4 - [4 - (β - ⟨3 - fluorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 210—212°C (decomposition) (from methanol/dimethylformamide),

ai) 4 - [4 - (β - ⟨3 - fluorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 198—200°C (from methanol) and

ak) 4 - [4 - (β - ⟨3 - fluorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - tetramethylene - semicarbazide, m.p. 200—202°C (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨3 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - methyl-urethane, m.p. 173—175°C

al) 4 - [4 - (β - ⟨3 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (1-methyl-pentamethylene) - semicarbazide, m.p. 210—211°C (from methanol/dimethyl formamide) and

am) 4 - [4 - (β - ⟨3 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1 - methyl - 1-isopropyl - semicarbazide, m.p. 176—177°C (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨4 - fluorobenzamido⟩ - ethyl) - benzenesulphonyl] - methyl-urethane, m.p. 194—196°C

an) N - [4 - (β - ⟨4 - fluorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 215—217°C (decomposition) (from methanol/dimethyl formamide);

from N - [4 - (β - capronamido - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 113—115°C

ao) 4 - [4 - (β - capronamido - ethyl) - benzenesulphonyl] - 1,1 - (3 - methylpentamethylene) - semicarbazide, m.p. 163—165°C (from methanol);

from N - [4 - (β - ⟨3 - ethoxy - thiophene - 2 - carbamido⟩ - ethyl - benzenesulphonyl] - methyl - urethane, m.p. 163—165°C,

ap) 4 - [4 - (β - ⟨3 - ethoxy - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 159—161°C (from methanol) and

aq) 4 - [4 - (β - ⟨3 - ethoxy - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 152—153°C (from methanol);

from N - [4 - (β - ⟨3 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 173—175°C,

ar) 4 - [4 - (β - ⟨3 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3-methyl - pentamethylene) - semicarbazide, m.p. 237—239°C (decomposition) (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨2 - ethoxybenzamido⟩ - ethyl) - benzenesulphonyl] - methyl-urethane, m.p. 172—174°C,

as) 4 - [4 - (β - ⟨2 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 153—154°C (from methanol),

at) 4 - [4 - (β - ⟨2 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 135—137°C (from methanol) and

au) 4 - [4 - (β - ⟨2 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (1 - methyl - pentamethylene) - semicarbazide, m.p. 137—139°C (from methanol);

from N - [4 - (β - ⟨2 - propoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 159—161°C

av 4 - [4 - (β - ⟨2 - propoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3-methyl - pentamethylene) - semicarbazide, m.p. 171—173°C (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 189—192°C,

aw) 4 - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl)benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 164—166°C (from methanol) and

ax) 4 - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 161—163°C (from methanol);
from N - [4 - (β - ⟨2 - methoxy - 4 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 178—180°C,
ay) 4 - [4 - (β - ⟨2 - methoxy - 4 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 177—179° (from methanol);
from N - [4 - (β - ⟨2 - methoxy - 3 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 151—153°C,
az) 4 - [4 - (β - ⟨2 - methoxy - 3 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 173—175°C (from methanol);
from N - [4 - (β - ⟨3 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 165—167°C,
ba) 4 - [4 - (β - ⟨3 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 207—208°C (decomposition) from methanol/dimethyl formamide),
bb) 4 - [4 - (β - ⟨3 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 177—179°C (from methanol/dimethyl formamide) and
bc) 4 - [4 - (β - ⟨3 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - 3 - methyl - pentamethylene) - semicarbazide, m.p. 224—226°C (decomposition) (from methanol/dimethyl formamide);
from N - [4 - (β - ⟨2 - methoxy - 5 - methylbenzamido⟩ - ethyl) - benzene - sulphonyl] - methyl - urethane, m.p. 175—177°C,
bd) 4 - [4 - (β - ⟨2 - methoxy - 5 - methylbenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 155—157°C (from methanol) and
be) 4 - [4 - (β - ⟨2 - methoxy - 5 - methylbenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 176—178°C (from methanol);
from N - [4 - (β - ⟨2 - β - methoxy - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 123—125°C,
bf) 4 - [4 - (β - ⟨2 - β - methoxy - ethoxy - benzamido⟩ - ethyl) - benzenesulph - onyl] - 1,1 - pentamethylene - semicarbazide, m.p. 143—145°C (from methanol) and
bg) 4 - [4 - (β - ⟨2 - β - methoxy - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl -pentamethylene) - semicarbazide, m.p. 157—159°C (from methanol);
from N - [4 - (β - ⟨2 - ethoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 203—205°C
bh) 4 - [4 - (β - [2 - ethoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 163—165°C (from methanol) and
bi) 4 - [4 - (β - ⟨2 - ethoxy - 5 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 164—166°C (from methanol);
from N - [4 - (β - ⟨2 - methoxy - 3 - methylbenzamido⟩ - ethyl) - benzene-sulphonyl] - methyl - urethane, m.p. 153—155°C
bk) 4 - [4 - (β - ⟨2 - methoxy - 3 - methylbenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene)semicarbazide, m.p. 170—172°C (from methanol);
from N - [4 - (β - ⟨2 - β - methoxy - ethoxy - 5 - methylbenzamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 160—162°C,
bl) 4 - [4 - (β - ⟨2 - β - methoxy - ethoxy - 5 - methylbenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 151—153° C (from methanol);
from N - [4 - (β - ⟨3 - chloro - phenoxy - acetamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 121—123°C
bm) 4 - [4 - (β - ⟨3 - chlorophenoxy - acetamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 106—108°C (decomposition) (from methanol);
from N - [4 - (β - ⟨β - 4 - chlorophenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 165—167°C
bn) 4 - [4 - (β - ⟨β - 4 - chlorophenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 179—181°C (decomposition) from methanol) and
bo) 4 - [4 - (β - ⟨β - 4 - chlorophenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 163—165°C (from methanol);

from N - [4 - (β - ⟨β - 3 - chlorophenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 128—130°C

bp) 4 - [4 - (β - ⟨β - 3 - chlorophenyl - propionamido⟩ - ethyl) - benzene - sulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 161—163°C (from methanol) and

bq) 4 - [4 - (β - ⟨β - 3 - chlorophenyl - propionamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 137—139°C (from methanol);

from N - [4 - (β - ⟨3,4 - tetramethylene - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - methyl - urethane, m.p. 194—196°C.

(br) 4 - [4 - (β - ⟨3,4 - tetramethylene - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 149—151°C (from methanol/dimethyl formamide) and

bs) 4 - [4 - (β - ⟨3,4 - tetramethylene - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 168—169°C (from methanol);

from N - [4 - (β - ⟨2 - methoxy - 3,5 - dichlorobenzamido⟩ - ethyl) - benzenesulphonyl] - urethyl - methane, m.p. 187—188°C

bt) 4 - [4 - (β - ⟨2 - methoxy - 3,5 - dichlorobenzamido⟩ - ethyl) - benzenesulphonyl] 1,1 - (3 - methyl - pentamethylene) - semicarbazide, m.p. 161—163°C (from methanol/dimethyl formamide);

from N - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - ethyl - urethane, m.p. 168°C

bu) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - (γ - dimethyl - pentamethylene) - semicarbazide, m.p. 155—157°C,

bv) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - (1 - iso-norgranatyl) - urea, m.p. 170—171°C,

bw) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (2,6-dimethyl - petamethylene) - semicarbazide, m.p. 203—204°C,

bx) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β-methyl - pentamethylene) - semicarbazide, m.p. 175—176°C,

by) N_1 - 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - N_2-[norgranatyl - (9)] - urea, m.p. 190—191°C,

bz) N_1 - 4 - [4-(β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl]-N_2-[nortropyl - (8)] - urea, m.p. 213—214°C,

ca) N_1 - 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - N_2-(1,2,5,6 - tetrahydropyridyl - 1) - urea, m.p. 156—157°C.

In an analogous manner there were obtained from the corresponding acylamino-ethyl - benzenesulphonyl - methyl - urethane

cb) 4 - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (α - methyl - pentamethylene) - semicarbazide, m.p. 185—186°C,

cc) 4 - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (α,α - dimethyl - trimethylene) - semicarbazide, m.p. 135°C,

cd) 4 - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - trimethylene) - semicarbazide, m.p. 196—197°C,

ce) 4 - [4 - (β - ⟨2 - methoxy - 5 - bromobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - trimethylene) - semicarbazide, m.p. 205—206°C,

cf) 4 - [4 - (β - ⟨2,5 - dimethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - trimethylene) - semicarbazide, m.p. 198—199°C,

cg) 4 - [4 - (β - (2 - methoxy - 5 - fluorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - trimethylene) - semicarbazide, m.p. 185°C,

ch) 4 - [4 - (β - ⟨2 - methoxy - 5 - fluoro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - pentamethylene) - semicarbazide, m.p. 115°C,

ci) 4 - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - pentamethylenee) - semicarbazide, m.p. 186°C,

ck) 4 - [4 - (β - ⟨2 - methoxy - 5 - bromobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - pentamethylene) - semicarbazide, m.p. 188°C,

cl) 4 - [4 - (β - ⟨2,5 - dimethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - pentamethylene) - semicarbazide, m.p. 154—155°C,

cm) - 4 - [4 - (β - ⟨4 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ-methyl - pentamethylene) - semicarbazide, m.p. 198—200°C,

cn) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β-methyl - tetramethylene) - semicarbazide, m.p. 161—162°C,

co) 4 - [4 - (β - ⟨2 - methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] -

1,1 - (β - methyl - pentamethylene) - semicarbazide, m.p. 167—168°C,
cp) 4 - [4 - (β - 〈2 - methoxy - 5 - chlorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - γ - (ethyl - pentamethylene) - semicarbazide, m.p. 157—159°C,
cq) 4 - [4 - (β - 〈2 - methoxy - 5 - chloro - benzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - pentamethylene) - semicarbazide, m.p. 191—193°C,
cr) 4 - [4 - (β - 〈2 - methoxy - 5 - chlorobenzamido〉 - ethyl) - benzenesulphonyl - 1,1 - (β - ethyl - pentamethylene) - semicarbazide, m.p. 180—181°C,
cs) 4 - [4 - (β - 〈2 - methoxy - 5 - bromobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ - ethyl - pentamethylene) - semicarbazide,
ct) 4 - [4 - (β - 〈2 - ethoxy - 5 - chlorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (β,β - dimethyl - pentamethylene) - semicarbazide,
cu) 4 - [4 - (β - 〈2 - methoxy - 5 - fluorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - pentamethylene) - semicarbazide, m.p. 160—162°C,
cv) 4 - [4 - (β - 〈2 - methoxy - 4 - chlorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - pentamethylene) - semicarbazide, m.p. 166—167°C,
cw) 4 - [4 - (β - 〈2 - methoxy - 5 - bromobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - pentamethylene) - semicarbazide, m.p. 182°C,
cx) 4 - [4 - (β - 〈2 - ethoxy - 5 - chlorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - pentamethylene) - semicarbazide, m.p. 162—165°C,
cy) 4 - [4 - (β - 〈2,5 - dimethoxy - benzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - pentamethylene) - semicarbazide, m.p. 170—171°C,
da) 4 - [4 - (β - 〈2 - methoxy - 5 - bromobenzamido〉 - ethyl - benzenesulphonyl] - 1,1 - (γ - ethyl - pentamethylene) - semicarbazide, m.p. 145—146°C,
db) 4 - [4 - (β - 〈2 - methoxy - 5 - fluorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ - ethyl - pentamethylene) - semicarbazide, m.p. 167°C,
dc) 4 - [4 - (β - 〈2,5 - dimethoxy - 5 - benzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ - ethyl - pentamethylene) - semicarbazide, m.p. 122—123°C,
dd) 4 - [4 - (β - 〈2 - methoxy - 5 - chlorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - trimethylene) - semicarbazide, m.p. 196—197°C,
de) 4 - [4 - (β - 〈2 - methoxy - 5 - bromobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - trimethylene) - semicarbazide, m.p. 205—206°C,
df) 4 - [4 - (β - 〈2,5 - dimethoxy - benzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - trimethylene) - semicarbazide, m.p. 198—199°C,
dg) 4 - [4 - (β - 〈2 - methoxy - 5 - fluorobenzamido〉 - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - trimethylene) - semicarbazide, m.p. 185°C.

Example 2

4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene-semicarbazide

a) 14.7 Grams of 4,4 - diphenyl - 1,1 - pentamethylene - semicarbazide were suspended with 16.3 grams of the sodium salt of 4 - (β - benzamido - ethyl) - benzenesulphonamide in 100 ml of dimethyl formamide and the whole was heated to 100°C for 3 hours. After cooling, the whole was diluted with water, the reaction mixture was rendered alkaline with ammonia and the diphenyl amine formed was removed by extracting three times with ether. The aqueous phase was filtered and acidified with glacial acetic acid. The 4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide precipitating in crystalline form, melted at 217—218° C after having been recrystallized from dimethyl formamide and water.

In analogous manner there was obtained

b) 4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide, m.p. 233—236°C (from dimethyl formamide/water).

Example 3

4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene-semicarbazide

a) 5.9 Grams of 1 - pentamethyleneimino - parabanic acid were suspended in 240 ml of benzene. After addition of 3 grams of trimethyl amine, the mixture was dissolved and 9.7 grams of 4 - (β - benzamido - ethyl) - benzenesulphochloride were added while stirring. The whole was refluxed for 3 hours, then cooled and decanted from the smeary residue. This residue was digested with water in order to remove the triethyl-amine hydrochloride formed, and was made to recrystallize by trituration with alcohol and water. The 1 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 3 - pentamethylene - imino - parabanic acid thus obtained was purified by boiling it with

methanol and it melted at 228°C (decomposition).

b) 0.5 Gram of the parabanic acid derivative obtained in the manner described above, was heated with 5 ml of 1N sodium hydroxide solution on the steam bath for 10 minutes. After a little while, the salt of 4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide crystallized out. It yielded the free compound, m.p. 218°C, by acidification with dilute acetic acid.

EXAMPLE 4

4 - [4 - (β - ⟨4 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide

9.5 Grams of N - [4 - (β - ⟨4 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl]-urea, m.p. 194—196°C, were refluxed at the boil in 100 ml of dioxane with 5 grams of N - amino - piperidine. After a limpid solution had been formed, the solvent was evaporated at reduced pressure, the residue was treated with about 1% ammonia and then filtered. The filtrate was acidified with dilute acetic acid. The 4 - [β - 4-chlorobenzamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide which had precipitated, was recrystallized from water and dimethyl formamide and it melted at 220—223°C (decomposition).

EXAMPLE 5

4 - [4 - (β - ⟨3 - methyl - 4 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide

a) 16.8 Grams of sodium 4 - (β - ⟨3 - methyl - 4 - chloro - benzamido⟩ - ethyl)-benzenesulphonamide were heated to 180°C with 11.1 grams of 1,1,5,5 - bis - pentamethylene - carbohydrazide, m.p. 178°C in a pre-heated oil bath for 10 to 15 minutes. The mixture became pasty and then solidified again. After having been cooled, it was treated with water, after filtration the filtrate was acidified with acetic acid and the reaction product was recrystallized from methanol. The 4 - [4 - (β - ⟨3 - methyl - 4-chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide melted at 204—206°C.

In analogous manner there were obtained:

b) 4 - [4 - (β - ⟨3 - methyl - 4 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - tetramethylene - semicarbazide, m.p. 174—176°C (from methanol/water) and from 4 - (β - ⟨α - methoxy - phenyl - acetamido⟩ - ethyl) - benzenesulphonamide, m.p. 167—169°C, and 1,1,5,5 - bis - pentamethylene - carbohydrazide

c) 4 - [4 - (β - ⟨α - methoxy - phenylacetamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 146—148°C.

EXAMPLE 6

a) 4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide

0.01 mol of N - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - methyl - urethane were heated to 110—120°C while stirring, in 135 ml of toluene with 0.01 mol of γ - methyl - pentamethylene - hydrazine. The methyl alcohol formed was distilled off. After heating for 2—3 hours, the whole was allowed to cool and the residue was filtered off with suction; it was dissolved and re-precipitated from Na_2CO_3 and HCl. The 4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl) - 1,1 - (γ - methyl-pentamethylene) - semicarbazide obtained melted at 212°C.

In analogous manner there were obtained:

b) 4 - [p - (β - benzamido - ethyl)benzenesulphonyl] - 1 - methyl - 1 - isopropyl-semicarbazide, m.p. 204°C,

c) 4 - [p - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - (γ - methoxy - pentamethylene) - semicarbazide, m.p. 212°C

d) 4 - [p - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - (γ - isopropoxy - pentamethylene) - semicarbazide, m.p. 210°C.,

e) N_1 - [p - (β - benzamido - ethyl) - benzenesulphonyl] - N_2 - [norgranatanyl - (9)]-urea, m.p. 229—230°C,

f) 4 - [4 - (β - acetamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 203°C,

g) 4 - [4 - (β - acetamido - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide, m.p. 187—189°C.

EXAMPLE 7

4 - [4 - (β - benzamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide

0.013 Mol of 4 - [4 - (β - amino - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide (prepared by hydrolysis of 4 - [4 - (β - acetylamino-ethyl)-benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 198—199°C) was heated to 35°C in 15 ml of chloroform with 0.024 ml of pyridine and 0.013 ml of benzoyl chloride for 6 hours. The residue was filtered off with suction and dissolved and re-precipitated from Na_2CO_3 and HCl. This compound melted at 216—218°C.

EXAMPLE 8

a) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide

0.01 Mol of 4 - [4 - (β - amino - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide were dissolved in 0.01 mol of 2N NaOH and 0.01 mol of 2-methoxy - benzoyl chloride was added dropwise while stirring. For complete reaction the whole was heated to 40°C for 2 hours. The substance which had precipitated was filtered off with suction and the residue was dissolved and reprecipitated from Na_2CO_3 and HCl. The substance melted at 156°C.

In analogous manner there were obtained:

b) 4 - [4 - (β - trimethyl - acetamido - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide, m.p. 187—189°C,

c) 4 - [4 - (β - ⟨3 - toluylamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl-pentamethylene) - semicarbazide, m.p. 234—235°C,

d) 4 - [4 - (β - ⟨3 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide, m.p. 223—224°C.

EXAMPLE 9

a) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ-methyl - pentamethylene) - semicarbazide

0.01 Mol of 4 - [4 - (β - amino - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl-pentamethylene) - semicarbazide, m.p. 187—189°C, prepared by hydrolysis of 4 - [4 - (β - acetylamino - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide, was added to 10 ml of pyridine and 0.01 mol of 2 - methoxy - benzoyl chloride was added dropwise. While heating, the reaction took place. The substance was allowed to stand for 12 hours and was then heated on the steam bath for 30 minutes. After having been cooled, it was poured onto ice, the precipitate was filtered off with suction, dissolved and reprecipitated from Na_2CO_3 and HCl. The pure substance melted at 164°C.

In analogous manner there were obtained:

b) 4 - [4 - (β - ⟨5 - chloro - 2 - methoxybenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide, m.p. 165—168°C,

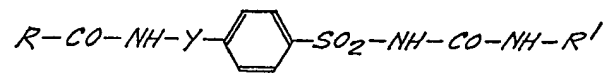
c) 4 - [4 - (β - ⟨3 - methoxy - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide, m.p. 174—177°C,

d) 4 - [4 - (β - ⟨2 - ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide, m.p. 169—171°C,

e) 4 - [4 - (β - ⟨2 - methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - ethyl - pentamethylene) - semicarbazide, m.p. 160°C, with sintering, m.p. 166°C

WHAT WE CLAIM IS:—

1. Benzene sulphonyl semicarbazides of the formula



wherein R represents

(a) a phenyl radical which may be unsubstituted or contain up to 3 substituents selected from lower alkyl, lower alkenyl, lower alkoxy, lower alkenoxy and lower alkoxyalkoxy radicals, halogen atoms and methylene - dioxy and trifluoromethyl,

(b) a thienyl radical which may be unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and lower alkyl, lower alkoxy, lower alkenyloxy, lower alkoxyalkoxy, phenyl - lower alkoxy and aryl radicals or by a polymethylene

chain linked at its two ends to the thienyl radical, which chain contains 3 or 4 carbon atoms,

(c) a furyl radical which may be unsubstituted or substituted by one or more substituents selected from halogen atoms and methyl groups,

(d) a phenyl radical bound via a saturated or unsaturated, branched or unbranched aliphatic hydrocarbon chain containing from 1 to 4 carbon atoms which may contain an oxygen atom instead of one CH_2-group, the phenyl radical containing, if desired, one or more substituents selected from halogen atoms and lower alkyl or lower alkoxy radicals,

(e) a cyclohexyl or cyclohexenyl radical, or

(f) an alkyl radical containing from 1 to 11 carbon atoms, or an unsaturated aliphatic hydrocarbon radical containing from 2 to 11 carbon atoms,

Y represents a $-CH_2-CH_2-$ or $-CH_2-\underset{\displaystyle CH_3}{\underset{|}{CH}}-$ group

R_1 represents

(a) an alkylene - imino radical containing from 3 to 7 carbon atoms wherein the alkylene chain may be substituted by 2 to 4 methyl groups or by an alkyl or alkoxy radical containing up to 3 carbon atoms, or

(b) an aliphatic hydrocarbon imino radical containing 5 carbon atoms which is unsaturated or contains an endoalkylene group having from 1 to 3 carbon atoms which may be substituted by lower alkyl or lower alkoxy, or

(c) the radical $-N<^{R_1}_{R_2}$, wherein R_1 represents a lower alkyl radical, and R_2 represents a lower alkyl or benzyl radical, and physiologically tolerable salts thereof.

2. 4 - [4 - (β - ⟨2 - Methoxy - 5 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ,γ - dimethyl - pentamethylene) - semicarbazide.

3. 4 - [4 - (β - ⟨2 - Methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - penamethylene) - semicarbazide.

4. 4 - [4 - (β - ⟨2 - Methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (β - methyl - pentamethylene) - semicarbazide.

5. 4 - [4 - (β - ⟨β - Phenylpropionamido⟩ - ethyl) - benzenesulphonyl] - 1,1-pentamethylene - semicarbazide.

6. 4 - [4 - (β - ⟨2 - Methoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1-pentamethylene - semicarbazide.

7. 4 - [4 - (β - ⟨2 - Ethoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1-hexamethylene - semicarbazide.

8. 4 - [4 - (β - ⟨2 - n - Propoxy - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide.

9. 4 - [4 - (β - ⟨2 - Methoxy - 5 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - pentamethylene - semicarbazide.

10. 4 - [4 - (β - ⟨2 - Methoxy - 5 - chlorobenzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide.

11. 4 - [4 - (β - ⟨2 - Methoxy - 4 - chloro - benzamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - (γ - methyl - pentamethylene)semicarbazide.

12. 4 - [4 - (β - ⟨3 - Methoxy - thiophene - 2 - carbamido⟩ - ethyl) - benzenesulphonyl] - 1,1 - hexamethylene - semicarbazide.

13. 4 - [4 - (β - ⟨2 - Methoxy - 5 - methyl - benzamido⟩ - ethyl) - benzene - sulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide

14. 4 - [4 - (β - ⟨2 - β - Methoxy - ethoxy - benzamido⟩ - ethyl) - benzene - sulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide.

15. 4 - [4 - (β - ⟨3,4 - Tetramethylene - thiophene - 2 - carbamido⟩ - ethyl) - benzene - sulphonyl] - 1,1 - (γ - methyl - pentamethylene) - semicarbazide.

16. Any one of benzene - sulphonyl semicarbazide as claimed in claim 1 and which is described in any one of the Examples herein, other than the compounds claimed in claims 2 to 15.

17. Physiologically tolerable salts of any one of the compounds claimed in claims 2—16.

18. A pharmaceutical preparation for oral administration and lowering the blood sugar level in the treatment of diabetes mellitus, which comprises a compound as

claimed in any one of claims 1 to 17 in admixture or conjunction with a pharmaceutically suitable carrier.

19. A pharmaceutical preparation as claimed in claim 18, which is in the form of a tablet.

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Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1968.
Published by the Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtained.